8/Declaration

Attorney Docket No. 219671USOCONT 1132

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN REAPPLICATION OF: :KEN HASSEN

: GROUP ART UNIT: 1615

SERIAL NO.: 10/073,978 : EXAMINER: TRAN, SUSAN T.

FILED: 02/14/2002

FOR: ULTRAFINE L-CARNITINE METHODS OF PREPARING THE SAME, COMPOSITIONS CONTAINING THE SAME AND METHODS OF USING.

DECLARATION UNDER 37 C.F.R. §1.132

ASSISTANT COMMISSIONER FOR PATENTS

WASHINGTON, D.C. 20231

SIR:

Now comes RAJ K. CHOPRA, who deposes and states that:

1. That I am a graduate of Gujarat University, India, and received my B.S. degree in Pharmacy (Honors) Gold Medalist, in the year 1965.

2. That I am also a graduate of Colombia University, and received my M.S. degree in Industrial Pharmaceutics in the year 1968.

3. That a copy of my curriculum vitae is attached hereto as Exhibit A and is incorporated into and is part of this declaration.

4. That I am currently the President and Chief Scientific Officer of Tishcon Corporation, Westburry, New York.

5. That I am a customer of Sigma-tau HealthScience Inc.

6. That I am using large quantities of ultrafine L-carnitine.

7. I do not receive compensation for my observations and comments within this declaration.

8. That I have reviewed the following:

   A. The specification and claims of U.S. Patent Application Serial No. 10/073,978 ("the '978 application");

   B. The Official Action dated June 4, 2002, in the 978 application;

and

C. U.S. Patent No. 4,602,039 (Cavazza)

D. U.S. Patent No. 6, 063,820 (Cavazza)

9. That is my opinion that the ultrafine L-carnitine described and claimed in the present application exhibits a number of unexpected advantages as compared to the L-carnitine described in Cavazza.

10. What was claimed in the '039 patent is a new non-hygroscopic salt of L-carnitine (for example L-carnitine fumarate). While L-carnitine fumarate in itself demonstrates an improvement in handling abilities over previous forms of carnitine for tabletting, it possesses a particle size and bulk density that is less than ideal for certain other applications, such as containment within hard and soft gelatin capsules. For this reason, many transformers rejected its use for hard and soft gel applications, choosing to remain with tablets. It was not obvious to reduce (micronize) the particles and use the specified flow agent, since this was felt unworkable, since carnitine in any form is not a candidate for particle reduction, since the frictional heat generated during the particle reduction process may induce the humid state relative to the ambient air temperature and thereby produce sticking. The trials by customers using regular L-carnitine fumarate vs. Ultrafine L-carnitine show that the finer, more free flowing characteristic of the latter finally allows blended content uniformity with other similarly particle sized ingredients, such as coenzyme Q10.

11. That my opinion is based on my experience and my use of both the ultrafine L-carnitine described and claimed in the present application and the conventional L-carnitine described in Cavazza. Specifically, I have used both conventional L-carnitine and ultrafine L-carnitine provided by Sigma-Tau Healthsciences in the formulation of dietary supplement dosage forms (soft gelatin capsules, hard gelatin capsules, and tablets) at Tishcon Corporation, and have found that ultrafine L-carnitine and salts thereof has a particle sufficiently small that substantially all of it passes through a 100 or 150, or 200 United State Bureau of Standards (USBS) mesh screen, while currently, L-carnitine and salts thereof prepared by the methods described in U.S. 4,602,039 yield L-carnitine having a size of such that greater than 10 % by weight of the L-carnitine is retained by a 50 mesh sieve and more than 40 % by weight is retained by a 100 mesh sieve; this characteristics renders ultrafine L-carnitine unexpectedly superior respect to the carnitine produced using the method described in U.S.

4,602,039.

12. The particle size reduction achieved with ultrafine L-carnitine has enabled Tishcon Corporation to design a soft-gel dosage form of ultrafine L-carnitine (for example fumarate) in combination with 1) omega-3 fatty acids in fish oil; 2) coenzyme Q10; and 3) alpha lipoic acid. The same good results have not been obtained using L-carnitine produced according to US 4,602,039.

13. The fineness of the particle size, as well as the particle size range of ultrafine L-carnitine, provides an ideal physical form to ensure content uniformity when filling multi-component active products in two piece hard gelatin capsules. Furthermore Tishcon Corporation has been able to obtain a high degree of color uniformity in its tables made with ultrafine L-carnitine. Particularly, in the soft gelatin encapsulation process, where the L-carnitine (for example fumarate) is processed into a paste with added vegetable oils, the particle size is a critical factor. Ultrafine L-carnitine performs perfectly in this process, while the conventional L-carnitine (for example fumarate) with its larger particle size range causes severe filling as well as sealing problems.

14. Due to the extremely fine state of subdivision afforded by ultrafine L-carnitine Tishcon Corporation is able to pack the powder more firmly in capsules, thereby leaving very little interstitial spaces between particles. This is probably the reason why these capsules do not exhibit premature:

1. Discoloration;
2. development of unacceptable odor;
3. moisture pick-up; and
4. physico-chemical instability

15. I declare further that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of this application or any patent issuing thereon.

DATE

March 7th, 2003

RAJK. CHOPRA

President

RAJ K. CHOPRA

Curriculum Vitae

Diploma, Pharmacy (Secured First position in the University, 1962)

B.S. Pharmacy (Honors) Gold Medalist, 1965 (Gujarat University, India)

M.S. (Industrial Pharmaceutics) Columbia University, 1968

Employment:

1977 - Present President and Chief Scientific Officer
Tishcon Corporation, Westbury, New York

1968 - 1977 Technical Director
PFI, Edison, New Jersey
(formerly Hempstead, New York)

1965 - 1968 Teaching Assistant, Columbia University
1967 Research Fellow (IFF), Columbia University
1966 Research Fellow (Sucrest Corp.), Columbia University

Experience:

34 years in the Nutritional Supplement Industry

Areas of Expertise:

- Formulation of solid, semisolid and liquid dosage forms.
- Taste and flavor masking of micro and macronutrients.
- Enhancing dissolution and bioavailability of nutrients.
- Formulating test supplements for clinical trials.

Publications:

"A new Coenzyme Q10 preparation with enhanced bioavailability."
R. Chopra, R. Goldman and H.N. Bhagavan
THE FASEB JOURNAL, Vol. II, No. 3, February 3, 1997.

"Evaluation of several materials as direct compression vehicles in pharmaceutical tableting." Thesis; 1968.

"Relative bioavailability of Coenzyme Q10 formulations in human

subjects."
R.K. Chopra, R. Goldman, S.T. Sinatra and H.N. Bhagavan
Int. J. Vitam. Nutr. Res., 1998; 68(2): 109-13

"Dietary Coenzyme Q10 and Vitamin E alter the status of these compounds
in rat tissues and mitochondria."
W.H. Ibrahim, H.N. Bhagavan, R.K. Chopra and C.K. Chow
J. Nutr, 2000 Sep; 130(9): 2343-2348

"Randomized, double-blind placebo-controlled trial of Coenzyme Q10 in patients with acute myocardial infarction."
R.B. Singh, G.S. Wander, A.Rastogi, P.K. Shukla, A. Mittal, J.P. Sharma

S.K. Mehrotra, Raj Kapoor and Raj K. Chopra
Cardiovascular Drugs and Therapy 1998; 12: 347-353

"Relative bioavailabilities of natural and synthetic Vitamin E formulations
containing mixed tocopherols in human subjects."
Raj K. Chopra and Hemmi N. Bhagavan
Internat. J. Vit. Nutr. Res., 69(2), 1999, 92-95

APhA - Poster Presentations

and several others.

Professional Memberships:

- American Pharmaceutical Association
- American Academy of Pharmaceutical Scientists
- Institute of Food Technologists
- National Nutritional Foods Association (corporate membership)